

**Medication Management
of
Community Based
Elderly People
in
Managed Care Organizations**

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I. Purpose

The purpose of this paper is to summarize the research literature about medication management and mismanagement for community based elderly enrollees in managed care organizations. Our focus is on studies about elderly people living independently in the community who are enrollees in managed care organizations; however, the research literature is limited all in three respects: (1) medication management and mismanagement for patients of any age, but especially for (2) community-based elderly, and (3) particularly for those enrolled in managed care organizations (MCOs) or health maintenance organizations (HMOs).

The four sections of this paper are the following:

- medication management -- the important components and who are the decision makers;
- medication mismanagement -- how is it defined and the extent of the problem;
- interventions for decreasing mismanagement of medications -- what interventions have been tried and which ones were found to be effective; and
- an ideal model of medication management for community based elderly who are enrollees in a managed care organization -- the assumptions and principal components and what research is needed to achieve an ideal model.

II. Medication Management

Definition of Medication Management. Medication management is a complex process that includes decisions and actions about: (1) selection of clinically effective drug treatment, (2) evaluation of the treatment for appropriateness and interactions, (3) dispensing of the medication, (4) use by the patient, (5) monitoring of medication effects, and (6) adjustment of treatment based on outcomes. Medication management is not solely a matter of compliance or adherence by the patient.

Components of Medication Management. Medication self-management can be further defined by the person most responsible for each component. These include:

- the physician or prescriber who is responsible for medication choice and prescription authorizing the dispensing of the medication, including over-the-counter drugs (OTCs), monitoring of side effects reported by the patient, and evaluation of health care outcomes;
- the pharmacist who is responsible for review of medication appropriateness and dosage, which includes an assessment of potential side-effects, interactions, dispensing the medication, and patient counseling about medication use and potential effects;
- the patient who is responsible for obtaining and using the medication at the prescribed dosage, schedule and duration, self monitoring for side effects or other adverse drug events, and communication with physician, pharmacist, or other health care team members about the effects and side-effects of the drug. The patient is also responsible for his or her own choice and use of self-selected OTCs and other medicinal preparations;

- other clinical providers in the health care organization, especially nurses, who are responsible for additional patient counseling or education; and
- individuals within the health care organization who are responsible for system decisions about formulary policies, drug choices, and premium and copay levels.

The role of the majority of these decision makers and the process of medication management are summarized in Figure 1. The decision makers for each component regarding medication management are management, i.e., the physician/prescriber, elderly patient, pharmacist, and managed care organization, are described in the next section.

(Insert Figure 1 here)

The focus of this paper is on community-based elderly people, i.e., those living in noninstitutional settings such as their own or family homes and not under the formal care of others. Self-management of medications can include the assistance of other people such as adult children, spouses, relatives or other informal care givers; but the emphasis here is on seniors willing and able to manage their own medication supervision. Additional issues about medication management include issues related specifically to the elderly population and variations in the definition of managed care organizations. Some of these issues include the following.

Elderly Populations. When the focus is on medication management by elderly people living independently in the community, then the complexity increases compared

to self-management by people in younger age groups. Factors contributing to this complexity among people 65 years and older include:

- increased number of chronic conditions requiring treatment.¹ Chronic conditions have been defined as illnesses that last longer than three months and are not self-limiting.² In 1993, 75% of the money spent on health care in the United States was for the treatment of chronic rather than acute illnesses;³
- compromised ability of elderly to metabolize and excrete some drugs and enhanced pharmacodynamic sensitivity;^{4 5} While the number of adverse drug effects does not increase simply as a function of age, the severity of the reactions is greater in the elderly;⁶
- increased cost of drug treatment;⁷
- both polypharmacy (use of multiple drugs) and greater comorbidity. While age itself has not proven to be an independent predictor of medication-related problems, polypharmacy is a significant risk factor;^{6, 8-11} as is the extent of comorbidity^{9, 10, 12}
- variations in patient compliance or adherence with the physician's recommendations for medication treatment or regimen.¹³

Managed Care Organizations. Health care delivery in a MCOs has the potential for improving medication management by community based elderly people, but only if the advantages of a coordinated system are in place and acted upon by health care providers. If the clinical, pharmaceutical, and financial databases are not integrated

and information is made available to health providers in an understandable and timely manner, then the MCO environment has few advantages over the less integrated fee-for-service sector in helping seniors with medication self-management. This definition of managed care includes those systems of health care provided by the Veterans Administration Medical Centers and in the Armed Forces.

The managed care market has matured over the past decade, although MCOs throughout the country differ widely in their organizational structures, diversity of health manpower, types of benefit plans (including availability of prescription benefits), and integration of clinical, pharmaceutical, and financial databases. Despite this diversity, there has been a discernible shift in concerns about pharmacy activities over the years, from an emphasis on cost control to that of patient outcomes.

For example, a model that summarizes the evolution of managed care pharmacy concerns was described by Flagstad¹⁴ in 1996 as comprising four phases. The first phase consisted of an emphasis on managing costs rather than managing care through benefit design, large-volume purchasing, and formulary restrictions. A second phase consisted of a focus on management of individual drugs through the use of prior authorization, drug utilization review (DUR) and drug use evaluation (DUE). Next, in Flagstad's hierarchy of emphases was the management of therapy of specific diseases through the use of disease stage management; and, fourthly, was a shift in emphasis to patient outcomes through the use of integrated datalinks of clinical, pharmaceutical, and financial databases. Flagstad believes that the fourth phase is the ultimate goal of all integrated health systems, whether managed care pharmacy is an internal part of an MCO or has been outsourced.

III. Medication Mismanagement

Definition of Medication Mismanagement. Optimal medication management requires appropriate prescribing by the physician, review and dispensing by the pharmacist, appropriate use of the medication by the patient, and follow-up through monitoring and counseling of the patient by the physician, the pharmacist, and other health care providers. Medication mismanagement consists of suboptimal prescribing (inappropriate, polypharmacy, or underuse), or errors in dispensing or patient errors in the use of medications (noncompliance or nonadherence). The following will address suboptimal prescribing and medication noncompliance, the most common problems.

Prevalence and Risk of Inappropriate Prescribing Among the Elderly. Inappropriate prescribing can be defined as the prescription of medications outside the bounds of accepted medical standards.¹⁵⁻¹⁷ This problem occurs commonly for elderly outpatients. In 1992, Lipton, et al, reported that 88% of 236 elderly ambulatory patients had one or more of the following problems with prescription medications: no indication, improper schedule, inadequate dosage, potential drug interaction, therapeutic duplication, or allergy.¹⁸ Twenty two percent of the patients were determined to have a serious problem with one or more categories. Another study of prescribing appropriateness in 208 ambulatory elderly veterans with polypharmacy found that 74% of the drugs taken by these older patients had at least one inappropriate rating.¹⁵ Several investigators have demonstrated, using explicit criteria developed by Beers et

al,¹⁹ that the use of 20 medications that should be avoided in elderly people occurs among 14% to 23% of persons 65 years of age and older living in the community.²⁰⁻²² The Beers criteria were recently revised and have been expanded to consider drug-disease interactions.²³

Other research suggests that medication inappropriateness is associated with drug-related hospital admissions and readmissions and higher medical care expenditures. For example, in one study, half of all adverse drug reactions causing hospital admissions in elderly patients were due to inappropriate prescribing of drugs because of contraindications or interactions.²⁴ In another study, 19% of drug-associated admissions in the elderly were related to one type of inappropriate prescribing, that of therapeutic failure or inadequate drug therapy.⁹ Bero et al, found that 29% of drug-related hospital readmissions were due to medication inappropriateness.²⁵ Another study documented that 50% of adverse drug reactions causing hospital admissions in elderly patients were due to drug-drug interactions.²⁶ A recent GAO report estimated that hospitalization due to inappropriate prescribing in the elderly costs \$20 billion annually.²²

Prevalence and Risk of Polypharmacy Among the Elderly. Polypharmacy, defined as concomitant use of multiple drugs, is common in elderly persons.^{27, 28} Community-based surveys reveal that elders take an average of 2.7 to 3.9 prescription and nonprescription medications.^{29, 30} The average number of drugs is somewhat higher in hospitalized elderly with an average of approximately five medications per patient at

discharge^{31, 29} Drug use is even higher in nursing facilities where institutionalized elderly take an average of 8.9 routine and prn medications.³² No specific number of medications has been established to define unnecessary polypharmacy; however, a HCFA indicator of nine or more medications on the Minimum Data Set (a standardized resident evaluation form) triggers further patient monitoring in nursing home facilities.³³

Polypharmacy has been identified in the federal government's Healthy People 2000 as one of the principal drug safety issues.³⁴ There is a strong, positive association between multiple medication use and adverse drug reactions.³⁵ The sequelae of multiple drug use may also increase utilization of health care resources and concomitant costs and have a negative effect on the patient's health related quality of life. Several studies in the literature provide empirical support for the association between polypharmacy and negative effects at the patient or health system level.

- A study of ambulatory patients in Australia found that polypharmacy was associated with multiple physician visits.³⁶
- In another study, in a sample of 300 patients referred to a tertiary care clinic for evaluation of cognitive impairment, 35 of the patients were rated as having drugs as the possible etiology of this condition; the study concluded that cognitive impairment was associated with increased numbers of medications.³⁷
- A prospective cohort study involving 609 community dwelling elderly women found that increased number of prescription medications, after controlling for age, education, and physical health, was associated with decline in ability to conduct

both physical and instrumental activities of daily living.³⁸ Moreover, the researchers found that increased number of nonprescription medications, after controlling for age, education, and physical health, was associated with decline in ability to conduct physical instrumental activities of daily living.

Prevalence and Risk of Underuse Among the Elderly. Underuse of medications in the elderly, defined as the omission of drug therapy that is indicated for the treatment or prevention of a disease or condition, is receiving increasing attention in the research literature. In a sentinel study that examined all forms of underuse, 55% of 236 ambulatory elderly patients had one or more necessary drug therapies omitted by lack of physician prescribing.³⁹ Other investigators have focused on the omission of treatment of certain conditions such as hypertension, cancer chemotherapy, depression and lack of preventative therapy, i.e., immunizations, beta blockers post myocardial infarction and antithrombotic therapy in patients with atrial fibrillation).^{40, 34, 41, 42, 43} Krumholz, et al, showed that only half of a sample of Medicare patients had beta blockers upon hospital discharge; the medication was noted in the medical record and no clinical contraindications were present.⁴³ A recent study pointed out that only 1/3 of nursing home patients with atrial fibrillation were being treated with warfarin.⁴²

Underutilization of appropriate medications has been associated with negative patient outcomes. For example, one study documented that limiting Medicaid patients access to medications more than doubled their risk of admission to nursing home⁴⁴ Similarly, this group of researchers found that limiting Medicaid drug-reimbursement

benefits for the use of psychotropic agents increased the use of mental health services by patients with schizophrenia.⁴⁵ Untreated depression has been shown to be associated with functional disability and health services utilization.³⁴ Mortality was also found to be 1.75 times more likely in elderly patients who had experienced a myocardial infarction and for whom beta blockers were indicated but not received.⁴⁶

Prevalence and Risk of Medication Noncompliance Among the Elderly. Medication noncompliance is a common problem in the elderly. The average noncompliance rate, when defined as an error with one or more medications, is 50% among elderly patients.^{47, 48} However, when noncompliance is defined as the proportion of drugs taken correctly elderly patients may be compliant with up to 75% of their medications, overall.⁴⁹ The rate of compliance among elderly patients is approximately the same as that of younger patients when the number of drugs taken by both groups is similar.⁵⁰ The most common type of noncompliance is underuse.⁵¹

Some authors have speculated that some patient noncompliance may be intentional and intelligent since it may be related to the occurrence of adverse drug reactions^{13, 48} Conversely, noncompliance may be associated with increased health services utilization. A study by Col, et al, evaluated 315 consecutive elderly patients admitted to a hospital and determined that 11.4% of admissions were due to noncompliance.⁵² A meta-analysis by Sullivan et al that included patients of all ages determined that the rate of hospital admissions due to noncompliance was 5.5%.⁵³

IV. Interventions for Medication Mismanagement

Overview: Search Strategies. Three electronic bibliographic databases, MEDLINE, International Pharmaceutical Abstracts, and HealthSTAR, were used in this literature review for the period 1987 to the present. Also used was the snowball technique of following up on lists of references in papers, whether the additional studies had been included in the three bibliographic databases or not. An earlier literature review of pharmacist interventions on medication management by the elderly was published in 1993 by Tett and her colleagues in which the search was limited to MEDLINE for the period 1975-1990.⁵⁴

This current review focused on patients as subjects. No studies were excluded by patient age, clinical condition (although most of the papers were on chronic conditions), medication, type of health care organization (most were not in managed care settings), or country in which the research was done.

Interventions. The 30 studies in which patients were the subjects of the intervention could be organized into the following seven categories:

- intensive multi-disciplinary care in either a specialty clinic⁵⁵ or a group educational and guidance program;⁵⁶
- home visit by one or more health care providers⁵⁷⁻⁵⁹ -- the two older studies took place in England;
- negotiating and/or contracting with patients about specific health behaviors or expected outcomes⁶⁰⁻⁶² -- all of these studies were with diabetes patients;

- patient counseling or educational materials,⁶³ including educational videotapes,⁶⁴ mail delivered programs,⁶⁵ and pharmacist counseling of hospitalized patients upon discharge;⁶⁶
- pharmacist monitored programs in outpatient settings;^{18, 67-72}
- medication adjustments by patients based on self-monitoring of blood levels^{73, 74} -- both studies were concerned with day to day monitoring of warfarin treatment; and
- training of patients in medication self-management of the condition⁷⁵⁻⁸³

Some of these 30 studies were descriptive only; of others that were empirically based, many were methodologically weakened by lack of a control group or sufficient sample size or statistical analysis.

Randomized Controlled Trials (RCTs). Fourteen of the 30 papers were more methodologically rigorous and included an experimental design with random assignment of subjects to experimental and control groups. We further categorized these 14 studies by one of three types of interaction, (1) patient education with video, mail, or booklet materials, (2) in-person interventions, and (3) intensive hands-on education/training/consultation with the patient. Figure 2 summarizes those 14 studies by these three types of intervention. Four of the studies^{62, 64, 65, 71} conducted in managed care settings are indicted in Figure 2 in bold print; all but two of the studies included subjects who were 65 years or older.

As shown in Figure 2, eight of the 14 RCTs showed statistically significant differences on a variety of outcome measures. In general, these results suggest that in

this set of studies, the more intensive the interaction between the patient and health care providers, the greater the likelihood of a statistically significant difference and improvement in the outcome variable, including improved patient compliance in medication self-management, reduced inappropriate prescribing by physicians, reduced costs, or lower health services utilization. Several of the studies showed improvement in patient adherence to the use of medications, but this adherence did not extend to a significant difference in reduction of hospital or emergency room admissions.

(Insert Figure 2 here)

V. An Ideal Model of Medication Management

Assumptions of an Ideal Model. An ideal model of medication management for independently living elderly people would begin with several assumptions including the following:

- Prescription Benefit -- a prescription benefit would be available to all enrollees that would not limit either the patient's access to treatment or number of medications per month. As described above, research has shown that formulary restrictions for medications used to treat five major disease groups were associated with higher yearly drug costs and drug counts,⁸⁴ and limits on the number of reimbursable prescription drugs resulted in increased number of hospital visits and nursing home admissions.⁴⁴

A prescription benefit might reasonably be expected to include a patient co-pay in order to offset some of the expense of the prescription benefit program. Previous

research in large HMO⁸⁵ demonstrated no consistent relationship between increased copayments and medical care utilization and expense. The study was limited by the use of a quasi-experimental design that did not include random assignment of subjects to groups.

- Integrated Database -- a managed care environment in which continuously up-dated electronic medical records about the patient would be available in an integrated database that could be accessed at any time by all health care providers, i.e., physician, pharmacist, nurses, and allied health providers. Such a database would make possible on-going feedback for clinicians as well as electronic drug utilization review which could be used to track prescriptions and intervene with inappropriate drugs and dosages.⁸⁶

Ideally such a database would include demographic information (including name, address, and telephone, number of informal caregivers who are specified by the patient), progress notes, vital signs, and medication information, including refill activities, laboratory and radiology results, and a record of the patient's use of health care services across delivery sites, e.g., clinic, day surgery, and hospital.

- Interdisciplinary Health Care -- an interdisciplinary approach to health care delivery in which communication within and among health care providers in different specialties and at different sites is seamless and cooperative. Previous research has suggested that pharmacotherapy can be improved through the use of multidisciplinary teams.⁸⁷

- Patient as Participant -- the inclusion of the patient, and, with his/her choice, informal caregivers or family members, in discussions about treatment choices.

The role of the patient in medical decision making has been discussed primarily in the social sciences literature.⁸⁸⁻⁹⁰ More empirical research is needed regarding the impact of the patient's participation in medical decision making, including medication choices, on patient compliance or adherence to the prescribed medications.

Elements of an Ideal Model. Given these assumptions, an ideal model of medication self-management would include the following components:

- Patient Education -- availability of patient education, perhaps in a group model as described by a pilot study⁵⁶ in Kaiser's Colorado-based Cooperative Health Care Clinic or perhaps pharmacy clinics or disease discussion groups with a nurse/pharmacist. In addition, patient education and counseling would be made available to all patients and their family/informal care providers upon hospital discharge and with each major change or addition of medication.

Empirical research is needed to demonstrate the effectiveness of group vs. individual vs. usual care in its impact on patient compliance or adherence to prescription medications. Despite an emphasis in the pharmacy literature on patient counseling and education by pharmacists, there is a lack of well controlled studies of either the effectiveness of such counseling or patient outcomes resulting from such interventions with elderly patients in their management of prescription

medications.⁵⁴ Such research also needs to take into account intentional nonadherence of medications by patients.¹³

- Targeting of High Risk Patients -- targeting by the MCO of the subset of patients at highest risk for medication mismanagement based on their complexity of conditions, medication regimens, or types of drug treatments that require daily monitoring. This subset of patients (and their family/informal caregivers) could be invited to participate in intensive hands-on education/training/consultation provided on a routine basis, e.g., monthly, quarterly, etc. Research is needed to demonstrate that such targeting of medication mismanagement and clinical follow-up is associated with reduction in adverse outcomes for high risk patients.
- Prescriber-Pharmacist Interaction -- Ongoing interaction between the physician or other prescriber and the pharmacist concerning drug treatment choices, including specific information about dosage and duration decisions that are based on the pharmacokinetics and pharmacodynamics of an elderly population. Previous research has demonstrated the effectiveness of some, but not all, methods used to influence physician choice of medications. The results of these studies, listed in Figure 2, are not consistent. This body of research needs to be taken to the next step by showing the impact on patient outcomes of the pharmacist's influence on physician prescribing behaviors. In other words, what impact does intervening with physicians and other prescribers by pharmacists or by other educational change agents have on patient variables?
- System-wide Knowledge and Annual Review of Drug Treatment -- annual analysis of prevalence of drug treatments of elderly and ability to target specific drugs for

further analysis, e.g., what proportion of the elderly enrollees have used SSRIs vs. tricyclic antidepressants over the past year and how did all costs related to mental health compare? Further research is needed concerning how managed care organizations make decisions about choice of drugs to include in the formulary, including the relationships between pharmaceutical company discounts and charges to enrollees.

- Formulary and Benefit Decisions Based on all Costs -- statistical analysis and econometric modeling of cost effectiveness of different drug treatments, taking into account costs throughout the health care delivery system, e.g., comparing total costs of a newer, more expensive drug compared to an older, cheaper drug when health services utilization is taken into account over a one year period. Feedback of these analyses to the MCO's Pharmaceuticals and Therapy Committee and others who make decisions about formulary choices and restrictions.

Little is known about whether or not managed care organizations consider the array of health care events over a specified period, e.g., over one calendar year, in making comparisons of the cost of drugs. For example, what kinds of inpatient and outpatient costs are included in comparing the total, yearly cost of using one drug compared to another within the same drug class? Such research needs to be multivariate and based on a sufficiently large sample size in order to adjust for patient attrition, including appropriate clinical discontinuation of the drug as part of the treatment plan.

These are some of the main elements that we believe should be considered in an ideal model of medication self-management by elderly enrollees in a managed care environment. The goal of such a model should be to make it possible for elderly people to use medication self-management in order to achieve clinical outcomes that are both cost efficient and insure their health related quality of life. The research that is needed should take into account patient, provider, and system level variables in examining factors associated with effective management and self-management of medications by elderly people.

Conclusions

Sufficient evidence in the research literature documents problems with the management of medications by and for elderly people, regardless of the health care system in which they are enrolled. There is less research, however, that describes the effectiveness of interventions designed to eliminate or correct such problems. This is especially true for research about interventions in which the subjects of the studies are elderly people who are living independently in the community and are enrollees in managed care organizations.

The management of medications has been defined as a complex process that includes physicians, pharmacists, other health care providers, such as nurses and health educators, patients, and individuals within the health care system who responsible for making decisions about the availability and pricing of medications. Research about the self-management of medications that focuses only on the patient's role in this process is restrictive. Such research needs to take into account the array of

individuals who interact with the patient and the roles they play. Likewise, studies of interventions in the mismanagement of medications needs to take into account not only the underuse and overuse of drugs, the suboptimal prescription of medications, but also the role of the patient in the choice and use of prescription and OTC drugs. In this paper, we have discussed four issues: a broad definition of medication management and mismanagement, research that addresses the problems of mismanagement, regardless of the health care system, interventions designed to decrease the management of medications, especially those studies that concentrated on the patient as the subject of the intervention, and an ideal model of medication management for elderly enrollees in a managed care organization.

**Figure 1. Decision-makers and Their Decisions
in the Process of Medication Management**

<u>Decision-maker</u>	Physician	Pharmacist	Patient	Health
Care				System
<u>Components of Decisions</u>	Selection of Drug Treatment and Interactions	Evaluation of Drug for Appropriateness	Use of Medication	Formulary Decisions
	Patient Counseling	Dispensing of Medication to Patient	Monitoring & reporting of reactions, side effects, & effective- ness	Decisions about premium & co-pay
	Monitoring of Side Effects;	Patient Counseling		
	Evaluation of treatment outcomes			

Figure 2. Comparison of Randomized Controlled Trials with Elderly Patients by Type of Intervention

Type of Intervention	Study	Condition	Statistical Effect & Direction ⁺
<u>Patient education</u>			
Mailed videotapes about medications	Powel, et al, 1995 ⁶⁴	Four specific medications [*]	NS: medication compliance
Mailed booklet about arthritis, including medications	Fries, et al, 1997 ⁶⁵	Arthritis [*]	Sig: ↑ pt outcomes; and ↓utilization
Booklet on self-management of condition	Watson, et al, 1997 ⁸⁰	COPD [*]	Sig: ↑ self-management by patients NS: quality of life scores or
pulmonary			function
<u>In-person intervention</u>			
Three randomly assigned groups vs. control: 1. Discussion with nurse about medication compliance 2. Self monitoring of behavioral strategies 3. Behavioral strategies condition with instruction & workbook	Boehm, et al, 1993 ⁶²	Type II diabetes [*]	NS: glycosylated hemoglobin or weight loss
Two randomly assigned groups vs. control: 1. Home visit by pharmacist & counseling on use & storage of meds 2. Home visit by pharmacist; no counseling	Begley, et al, 1997 ⁵⁸	not condition specific [*]	Sig: ↑ drug knowledge by Gp 1 only
Home-based intervention	Stewart, et al, 1998 ⁵⁷	CHF [*]	Sig: ↓ hosp re-admission

Booklet, 1:1 counseling, adherence-enhancing strategies	Bailey, et al, 1990 ⁶³	Asthma [*]	Sig: ↑ adherence to medications ↑ functional status
<u>Intensive hands-on</u>			
Pharmacists' consultations	Lipton, et al, 1992 ¹⁸	generic meds for [*] chronic conditions	Sig: ↑ appropriate drug regimen
Self-management program taught by lay leaders & booklet	Lorig, et al, 1993 ⁷⁸	arthritis [*]	NS: no difference
Patient education, dietary, social service consultation, medication review, and follow-up	Rich, et al, 1996 ⁸³	CHF [*]	Sig: ↑ medication compliance
Pharmacist intervention	Hanlon, et al, 1996⁷¹	polypharmacy [*]	Sig: ↓ inappropriate prescribing NS: health related quality of life
Self-management & personal education	Lahdensuo, et al, 1998 ⁷⁵	asthma	Sig: ↓ indirect costs, ↓ total costs, ↑ healthy days
Self-management days lost, management of asthma days ↓ ER visits, indirect costs	Ghosh, et al, 1998 ⁷⁶ training in manage-	asthma	Sig: ↓ productive ↓ hospital ↓ total &
Self-management of asthma health life	Kauppinen, et al, 1998 ⁷⁷	asthma [*]	Sig: ↑ forced expiratory volume NS: clinical or related quality of variables
⁺ Statistical significance of p<.05; direction of statistical significant findings: = increased or improved,			

↓ = decreased or worse

References in **bold** indicate studies conducted in managed care settings, including the Veterans Administration Medical Centers

* Asterisk indicates studies that included (but were not limited to) subjects who were 65 years or older

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